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## Surgical management for upper tract transitional cell carcinoma

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# **Surgical management for upper tract transitional cell carcinoma (Protocol)**

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[Intervention Protocol]

# Surgical management for upper tract transitional cell carcinoma

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## ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To determine the best surgical management of upper tract transitional cell carcinoma.

The following comparisons are pre-stated:

1. Whether open radical nephroureterectomy is better than laparoscopic nephroureterectomy
2. Whether nephroureterectomy is better than conservative localised resection of ureter, where indicated
3. Whether open surgical resection (local or nephroureterectomy) is better than endoscopic resection and surveillance, where indicated
4. Whether open surgical method of handling lower end of ureter is better than endoscopic or laparoscopic assisted methods

## BACKGROUND

Upper tract transitional cell carcinoma (TCC) arises from the renal pelvis, calices and ureters. These tumours are uncommon and constitute only 5% of TCCs of the entire renal tract (Campbell-Wash 2003). TCCs of the renal pelvis account for 10% of all renal tumours and ureteric TCCs are even less common (El-Fettouh 2002). Bilateral disease is extremely rare and occurs in 2% to 4% of the cases (Browne 2005). Although histologically similar to bladder TCCs, upper tract transitional cell carcinoma is more aggressive tumours with a tendency to multifocality, local recurrence and progression to an advanced stage (David 2002; Browne 2005; Muntener 2007).

The risk of upper tract TCCs increase with age and commonly occur between the sixth and seventh decade of life. Men have a two to three times more risk of developing upper tract TCCs as compared to women (David 2002; Campbell-Wash 2003). Cigarette smoking is the most significant acquired risk factor for upper-tract TCCs (Jensen 1988; McLaughlin 1992). Balkan endemic nephropathy (Petkovic 1975), analgesic abuse (particularly phenacetin) (McCredie 1982), exposure to chemical, petrochemical, aniline dye, coal, coke, tar, asphalt and plastic industry workers (Jensen 1988), chronic bacterial infection, and chemotherapy drugs (cyclophosphamide and ifosfamide), have all been implicated.

Upper tract transitional cell carcinoma is rarely asymptomatic. Frank or microscopic haematuria is the commonest presentation followed by loin pain (Campbell-Wash 2003). Other clinical presentations include renal colic, palpable mass, weight loss, anorexia, and bone pain (Campbell-Wash 2003).

Diagnosis is based on clinical, cytological, endoscopic and imaging grounds (Johnson 2005; Painter 2007). Useful imaging modalities include, retrograde pyelography, renal USS, CT and MR Urography (Browne 2005). Stage and grade at presentation dictate prognosis, with staging being the single most important prognostic indicator (Olgac 2004).

Open nephroureterectomy (ONU) has been the standard surgical option for upper-tract TCCs with a normally functioning contralateral collecting system. The procedure itself consists of total nephroureterectomy with excision of the bladder cuff around the ureteric orifices to prevent tumour recurrence in the ureteric stump or around the ipsilateral ureteric orifice. The procedure entails either two long incisions or single long incisions for adequate exposure. As a result there is significant morbidity in the form post-operative pain and therefore prolonged hospitalisation (Rassweiler 2004).

There has been considerable advancement in minimal invasive surgery in recent years to counter issues of post-operative pain, prolonged hospitalisation associated with ONU. Some of the viable options include laparoscopic nephroureterectomy (LNU), ureteroscopic resection/fulguration or percutaneous management.

Reports have proven that LNU that has reduced morbidity significantly as compared to ONU and the long term oncological efficacy of LNU are similar to ONU (David 2002; El-Fettouh 2002; Bariol 2004; Rassweiler 2004; Arancibia 2007; Busby 2007; Muntener 2007). For these reasons LNU is steadily becoming the standard procedure of choice for upper tract TCCs especially bulky, large sized tumours in various centres.

With the recent development of sophisticated ureteroscopes, endoscopic management of low grade lesions measuring <1.5 cm with normal contralateral kidneys has been reported in various studies to be a very favourable option (David 2002; Johnson 2005; Soderdahl 2005; Mugiya 2006). However the need for long-term surveillance and patient suitability are limiting factors. Laser therapy and electrocautery are the commonly used modes in these settings. Adjuvant topical therapy (mitomycin, BCG, etc) has been suggested to reduce recurrence of disease following endoscopic therapy (Keeley 1997).

Percutaneous approach combined with resection of the tumours has been suggested in some reports to be a useful option in low grade, large tumours (Jabbour 2000; Soderdahl 2005). For patients with solitary, bilateral tumours, severe renal insufficiency and severe co-morbidities, partial nephrectomy, segmental ureteral resection with re-anastomosis or ureteroscopic management, are surgical options. (Campbell-Wash 2003; Johnson 2005).

Furthermore, there are various techniques described to deal with the lower end of the ureter during nephroureterectomy such as open excision, laparoscopic or endoscopic assisted methods. However there is no consensus on the best way to deal with lower end and surgical practice remains an issue of surgeon's preference and experience.

## OBJECTIVES

To determine the best surgical management of upper tract transitional cell carcinoma.

The following comparisons are pre-stated:

1. Whether open radical nephroureterectomy is better than laparoscopic nephroureterectomy
2. Whether nephroureterectomy is better than conservative localised resection of ureter, where indicated
3. Whether open surgical resection (local or nephroureterectomy) is better than endoscopic resection and surveillance, where indicated
4. Whether open surgical method of handling lower end of ureter is better than endoscopic or laparoscopic assisted methods

## METHODS

## Criteria for considering studies for this review

### Types of studies

All randomised or quasi-randomised controlled trials comparing the various surgical methods and approaches for the management of localised upper tract transitional cell carcinoma.

### Types of participants

All adult patients with localised transitional cell carcinoma. Localised disease is defined as limited to the kidney or ureter with no gross lymph nodal enlargement on imaging.

### Types of interventions

Any surgical method or approach for managing localised renal cell carcinoma.

### Types of outcome measures

Various outcomes of interest are:

#### EARLY SURGICAL OUTCOME

Need for re-operation  
Operative complications  
Post-operative morbidity / mortality  
Length of operation  
Length of hospital stay  
Duration of catheterization  
Analgesic requirement  
Positive surgical margins (local resection of ureter)

#### CANCER OUTCOME MEASURES

Overall survival  
Cancer-specific survival  
Positive margin rate  
Incidence of local recurrence or progression  
Incidence of distant metastasis

#### HEALTH-RELATED QUALITY OF LIFE (HRQOL) OUTCOME MEASURES

Generic HRQOL measures (e.g. SF-36 Ware 1992)  
Disease-specific HRQOL measures (e.g. UCLA PCI Litwin 1998)

#### HEALTH ECONOMIC OUTCOME MEASURES

Resource implications of differences in outcomes  
Resource implications of differences in impact on HRQOL  
Formal economic analysis (cost utility)  
Length of hospital stay (days) and associated costs (in GBP)

### Search methods for identification of studies

A sensitive search strategy will be developed to identify relevant studies for inclusion in this review. The following search terms will

be used in conjunction with the Cochrane highly sensitive search strategy for RCTs as described in the Cochrane Handbook for Systematic Reviews of Interventions (designed in OVID version of MEDLINE).

1. exp Carcinoma, Transitional Cell/
2. exp Ureteral Neoplasms/
3. ((upper tract or renal pelv\$ or ureter\$ or calice\$) adj3 (transitional or carcinoma\$ or tumor\$ or cancer\$ or neoplas\$)).tw.
4. or/1-3
5. exp Surgery/
6. nephroureterectomy.tw.
7. ((ureteral or percutaneous or surgical or ureteroscopic or endoscopic) adj3 (resection or management or fulguration)).tw.
8. (ONU or LNU).tw.
9. ((radical or open or laparoscop\$) adj3 (surg\$ or nephro\$ or nephrec)).tw.
10. partial nephrectomy.tw.
11. exp Electrocoagulation/
12. exp Laser Therapy/
13. re-anastomosis.tw.
14. electrocaut\$.tw.
15. or/5-14
16. 4 and 15

This MEDLINE strategy will then be translated and the following electronic databases searched:

1. EMBASE
2. Cochrane Library
3. CINAHL
4. British Nursing Index
5. AMED
6. LILACS
7. Web of Science
8. Scopus
9. Biosis
10. TRIP
11. Biomed Central
12. Dissertation Abstracts
13. ISI proceedings

In addition, trial registers and a variety of internet sites will be searched looking for meeting abstracts and other grey literature.

### Data collection and analysis

The literature search will be screened, and by consensus, relevant articles retrieved using above search strategy. Data will be extracted from each identified paper independently by two or more reviewers and cross checked. The extracted data will include information on trial design, participants, the type of intervention and outcome measures. Data analysis will compare radical surgery with other primary surgical modalities and comparisons made for each outcome. Also comparisons will be made between different surgical

approaches. The quality of each trial will be graded according to the concealment of allocation and adequate descriptions of numbers and reasons for patient withdrawal as detailed in the Cochrane Handbook.

The data analysis will be performed using Review manager. Comparable data from each trial will be combined in a meta-analysis where possible. For dichotomous data, relative risks (RRs) with 95% confidence intervals (CI) will be estimated based on the fixed effects model (and on the random effects model when heterogeneity is present) and according to an intention to treat analysis. Continuous outcomes will be analyzed if the mean and standard deviation of endpoint measures are presented. For the meta-analysis of continuous outcomes, weighted mean differences (WMDs) between groups will generally be estimated.

## WHAT'S NEW

Last assessed as up-to-date: 21 April 2008.

8 May 2008	Amended	Converted to new review format.
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## HISTORY

Protocol first published: Issue 4, 2008

21 February 2008	New citation required and major changes	Substantive amendment
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## DECLARATIONS OF INTEREST

None.